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2002/M018 (A66)
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Claims:

1. Modified human factor VIII cDNA wherein mutations are inserted either in the wild-type factor VIII cDNA or in a factor VIII cDNA in which the B-domain is partially or completely deleted and may be replaced by a DNA linker segment, **characterised in that**

A) one or several codons of the human factor VIII cDNA which are not identical with the corresponding codon in the same position of the porcine factor VIII cDNA are substituted by a different codon in such a way that

- when the human sequence contains a codon for a neutral amino acid whereas the porcine sequence contains a codon for a charged amino acid then a codon for an amino acid with the same charge as found in the porcine sequence is introduced into the human sequence;

- when the human sequence contains a codon for a charged amino acid whereas the porcine sequence contains a codon for a neutral amino acid then a codon for a neutral amino acid or a codon for an amino acid of the opposite charge is introduced into the human sequence,

- when the human sequence contains a codon for a charged amino acid whereas the porcine sequence contains a codon for an amino acid with the opposite charge then a codon for an amino acid with the opposite charge is introduced into the human sequence or

B) one or several codons for a charged amino acid which are found in the FVIII cDNA of a hemophilic patient are replaced by a codon for an amino acid of the opposite charge.

2. Recombinant expression vector containing the factor VIII cDNA as claimed in claim 1, **characterised in that** it carries in addition transcriptional regulatory elements for expression in a suitable host cell.

3. Modified biologically active recombinant human factor VIII with improved stability wherein mutations are inserted either in the wild-type factor VIII or in a factor VIII in which the B-domain is partially or completely deleted and may be replaced by a linker, **characterised in that**

A.) one or several amino acids of the human factor VIII which are not identical with the corresponding amino acid in the same position of the porcine factor VIII are substituted by a different amino acid in such a way that

- when the human sequence contains a neutral amino acid whereas the porcine sequence contains a charged amino acid then a charged amino acid with the same charge as found in the porcine sequence is introduced into the human sequence;

- when the human sequence contains a charged amino acid whereas the porcine sequence contains a neutral amino acid then a neutral amino acid or an amino acid of the opposite charge is introduced into the human sequence;

- when the human sequence contains a charged amino acid whereas the porcine sequence contains an amino acid with the opposite charge then an amino acid with the opposite charge is introduced into the human sequence or

B) one or several charged amino acids which are found in the FVIII amino sequence of hemophilic patients are replaced by a codon for an amino acid of the opposite charge.

4. Modified biologically active recombinant human factor VIII as claimed in claim 3, wherein the plasma half life of its activated form is more than 3 minutes, preferably more than 10 minutes and most preferably more than 30 minutes.

5. Modified human factor VIII, **characterised in that** its A2-domain is stabilised by the substitution of one or several amino acids as claimed in claim 3.

6. Process for the recombinant production of a modified human factor VIII as claimed in claim 3 either in cell suspension or on a solid support as a bath cell culture or as a perfusion cell culture with continuous production of a conditioned medium **characterised in that** the factor VIII proteins, which are expressed by a suitable host cell line are purified by chromatographic methods.

7. Process as claimed in claim 6, **characterised in that** the transcription units encoding the modified factor VIII cDNA of claims 1 and 2 contain a dominant selectable marker in order to facilitate the isolation of specific cell clones which have integrated said specific c-DNA into their genome.

8. Host cell line for expression of the factor VIII proteins of claim 3, **characterised in that** it is an animal cell line of vertebrate origin which contains the factor VIII cDNA of claim 1 integrated into its genome.

9. Pharmaceutical composition, **characterised in that it** comprises a modified biologically active recombinant human factor VIII of claim 3.

10. Vector for gene therapy of hemophilia A, characterized in that it contains a modified FVIII cDNA as claimed in claim 1.